Claims

1) Thrombin-conjugated nanoparticles, wherein said nanoparticles comprise one or more organic and/or inorganic compounds.

2) The thrombin-conjugated nanoparticles according to claim 1, wherein the thrombin molecules are covalently-bonded to the surface of the nanoparticles.

3) The thrombin-conjugated nanoparticles according to claim 1, wherein the thrombin molecules are covalently-bonded to spacer arms, and wherein said spacer arms are covalently-linked to the surface of the nanoparticles.

4) The thrombin-conjugated nanoparticles according to claim 1, wherein the thrombin molecules are physically adsorbed onto spacer arms, and wherein said spacer arms are covalently-linked to the surface of the nanoparticles.

5) The thrombin-conjugated nanoparticles according to claims 1 to 4, wherein the organic compounds are selected from the group consisting of proteins and synthetic polymers, and wherein the inorganic compounds are selected from the group consisting of metal oxides or oxides of metalloids.

6) The thrombin-conjugated nanoparticles according to claim 5, wherein the nanoparticles are selected from the group consisting of magnetic iron oxide-containing nanoparticles, albumin nanoparticles, solid or hollow silica nanoparticles and nanoparticles made of organic

polymeric core coated with a silica shell, optionally having magnetic layer interposed between said core and said silica shell.

7) The thrombin-conjugated nanoparticles according to claim 2, wherein the nanoparticles are magnetic iron oxide-containing nanoparticles having a coating on their surface, and wherein the thrombin molecules are covalently-linked to said coating.

8) The thrombin-conjugated nanoparticles according to claims 3 and 4, wherein the spacer arm is albumin.

9) The thrombin-conjugated nanoparticles according to any one of claims 1 to 8, further comprising a pharmaceutical agent, wherein said pharmaceutical agent is either encapsulated within said nanoparticles, or bound thereto.

10) A process, which comprises:
providing nanoparticles comprising one or more organic and/or inorganic compounds, said nanoparticles having reactive chemical groups on their surface, and either covalently linking thrombin thereto, or covalently linking spacer arms to said reactive chemical groups and subsequently allowing thrombin molecules to chemically react with said spacer arms, or to become physically adsorbed thereto, whereby thrombin-conjugated nanoparticles are obtained.

11) The process according to claim 10, wherein the reactive chemical groups are either activated carbon-carbon double bonds or aldehyde groups.

12) The process according to claim 11, which comprises covalently linking thrombin molecules to the nanoparticles by allowing the primary amine groups of the thrombin molecules to react either with the activated carbon-carbon double bonds via a Michael addition reaction, or with the aldehyde groups through the formation of Schiff Bases.

13) The process according to claim 11, which comprises covalently linking spacer arms to the nanoparticles by allowing primary amine groups of the spacer arms molecules to react either with the activated carbon-carbon double bonds via a Michael addition reaction or with the aldehyde groups through the formation of Schiff Bases, and subsequently allowing primary amine groups of the thrombin molecules to react with carboxyl groups of said spacer arms.

14) The process according to claim 10, wherein the spacer arm is albumin.

15) A therapeutic composition comprising a therapeutically effective amount of thrombin-conjugated nanoparticles as defined in claims 1 to 9, suitable for use in the preparation of fibrin-based biological sealant.

16) The therapeutic composition according to claim 15, provided in the form of a dry powder comprising thrombin-conjugated nanoparticles and a dispersant.

17) The therapeutic composition according to claim 16, wherein the dispersant is gelatin.

18) A therapeutic composition according to claim 15, provided in the form of a liquid vehicle comprising thrombin-conjugated nanoparticles and optionally a dispersant.

19) A therapeutic composition according to any one of claims 15 to 18, which further comprises one or more additives selected from the group consisting of Ca salts, factor XIII and antifibrinolytic agents.

20) A process for preparing a thrombin formulation provided in the form of a dry powder comprising thrombin-conjugated nanoparticles, said process comprising providing an aqueous suspension of said thrombin-conjugated nanoparticles and drying said aqueous suspension in the presence of a suitable dispersant.

21) The process according to claim 20, wherein the drying is accomplished by means of lyophilization.

22) The process according to claim 21, wherein the dispersant is gelatin.

23) The process according to claim 21, wherein the weight ratio of gelatin to thrombin-conjugated nanoparticles in the aqueous suspension is in the range of 1:2 to 2:1.

24) The process according to any one of claims 20 to 23, wherein the aqueous suspension containing the thrombin-conjugated nanoparticles and the dispersant is absorbed

onto a suitable support, said support being preferably in the form of cellulose, collagen or gelatin sheets, following which said support is dried to produce a dry powder of thrombin-conjugated nanoparticles thereon.

25) A method for preparing fibrin-containing biological sealant, wherein said method comprises contacting fibrinogen with a therapeutically effective amount of thrombin-conjugated nanoparticles as defined in claims 1 to 9 in a liquid medium selected from the group consisting of aqueous solution, plasma or blood, whereby the fibrin sealant is formed.

26) The method according to claim 24, which comprises contacting fibrinogen with a dry powder comprising thrombin-conjugated nanoparticles and a dispersant, or with a liquid suspension of said nanoparticles.

27) The method according to claim 25, wherein the dispersant is gelatin.

28) The method according to any one of claims 23 to 25, wherein the thrombin-conjugated nanoparticles and fibrinogen are contacted in the presence of calcium ions or factor XIII.